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RESEARCH ARTICLE

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Incidence and predictors of postoperative delirium after cytoreduction surgery-hyperthermic intraperitoneal chemotherapy

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Background: Incidence of, and baseline characteristics associated with delirium in patients after cytoreduction surgery-hyperthermic intraperitoneal chemotherapy (CRS-HIPEC), were subject of investigation.

Methods: The study was conducted among a consecutive series of prospectively included patients who underwent CRS-HIPEC at the University Medical Center Groningen, Groningen, the Netherlands, between February 2006 and January 2015. A chart-based instrument for delirium during hospitalization was used to identify patients with symptoms of delirium who were not diagnosed by a psychiatrist during admission. Uni- and multivariate logistic regression analyses were performed.

Results: Data of 136 patients were included in the analysis. Median age was 60 years (range: 18-76) and 50 (37%) patients were male. During hospitalization, 38 (28%) patients were diagnosed with delirium. Factors that differed significantly between the patients with and without delirium by univariate analysis were included in multivariate analysis. Multivariate analysis showed that after adjustment for age and complications other than delirium, having three or more organs resected and the CRP serum levels were independent predictors for delirium (OR: 3.97; 95% 1.24-12.76; OR: 1.01; 95% 1-1.01, respectively).

Conclusions: This report shows an incidence of 28% of delirium, occurring after CRS-HIPEC and suggests a role for systemic inflammation in the development of postoperative delirium.

KEYWORDS
cognition disorders, C-reactive protein, cytoreduction surgical procedures, delirium, neoplasm, postoperative complications

1 | INTRODUCTION

As systemic chemotherapy does not offer the possibility of cure in the treatment of peritoneal tumor dissemination in colorectal carcinoma, novel therapies have been developed. Cytoreduction surgery combined with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) is now the recommended treatment option for many peritoneal surface malignancies.[1,2] The purpose of cytoreduction is to obtain a

macroscopically complete resection, followed by intraperitoneal hyperthermic chemotherapy to treat any microscopic residual disease.[3] Current indications for CRS-HIPEC include non-invasive peritoneal carcinomatosis or sarcomatosis, peritoneal mesothelioma, perforated gastrointestinal cancers, gastrointestinal cancer adherent to adjacent organs, or structures and gastrointestinal cancer with positive peritoneal cytology.[4] The advent of CRS-HIPEC has changed the treatment perspective toward a curative approach for selected patients with colorectal peritoneal malignancy, peritoneal mesothelioma, or pseudomyxoma peritonei, now increasingly considered to be a loco regional manifestation of disease rather than an end-stage terminal event.[5]

CRS-HIPEC is a complex and time-consuming procedure and the treatment can have a considerable effect on the patient's general condition. The effects can be on the respiratory, cardiovascular, electrolyte, and metabolic status, and lead to a high perioperative morbidity and prolonged hospitalization.[6,7] Mental status may also be affected resulting in delirium, an acute confusion disorder characterized by an altered level of consciousness, inattention, and disorganized thinking. This change in cognition or perceptual disturbance develops over a short period of time (hours to days) and may fluctuate over the course of a day. Delirium can be classified into three subtypes, namely, hyperactive, hypoactive, or mixed.[8]

Although the pathophysiology of delirium remains largely unknown, it is generally accepted that the etiology involves multiple factors of different significance.[9,10] Consistent evidence is accumulating for the role of inflammatory processes arising due to surgical trauma and subsequent complications.[11] Research indicates that neuroinflammation plays a major role in the development of delirium.[12] It seems reasonable to expect that delirium is a frequent complication after CRS-HIPEC as this procedure is expected to cause a strong inflammatory response. However, few studies have reported on this specific postoperative complication. As delirium is associated with increased morbidity and mortality, it is certainly a complication to be avoided or timely recognized.[13] The purpose of this retrospective analysis is to identify the incidence of, and baseline characteristics associated with, delirium in a consecutive series of patients after CRS-HIPEC.

2 | PATIENTS AND METHODS

2.1 | Patients and design

The study is a retrospective analysis of a consecutive series of prospectively included patients who underwent CRS-HIPEC surgery at the University Medical Center Groningen (UMCG), Groningen, the Netherlands, between February 2006 and January 2015. This study was approved by the local medical ethical committee and privacy was guaranteed by coding data. A prospective database was sustained, containing patient and tumor-specific data. Data included demographic characteristics, medical history, surgical procedure, diagnosis, and length of hospital stay.

2.2 | Data acquisition

Data collected included body mass index (BMI), American Society of Anesthesiologists score (ASA), number of packed cells transfused, length of surgery, tumor type, peritoneal cancer index (PCI), number of organs resected during surgery, and completeness of cytoreduction (CC) score. The blood serum levels of C-reactive protein (CRP) during hospitalization after the CRS-HIPEC were retrieved from the hospital's data center. To identify and rank the postoperative complications, the Clavien Dindo complication classification (CDCC) was used. The (age adjusted) Charlson comorbidity index (CCI), an index in which each medical condition is assigned a weighted score (range 0-19), was used to quantify the medical comorbidity. To see which patients developed a delirium or mental status change during admission, charts of all patients were reviewed.

2.3 | Chart-based instrument for delirium during hospitalization

In certain patients, delirium was diagnosed by a psychiatrist or specialist in elderly medicine and registered as a postoperative complication during admission. To identify patients with symptoms of delirium during admission who were not conspicuous during that time, the chart-based instrument for delirium during hospitalization was used retrospectively. The chart-based instrument was created with the goal of maximizing sensitivity for identification for delirium and prompts the chart abstractor to search for key terms of identification for delirium, particularly searching for any evidence of acute mental status change. The chart-based instrument is not recommended for individual patient care, but it is suitable for institutional reporting about delirium.[14,15] All sections of the charts were searched, including but not restricted to progress notes, nursing notes, and consultant notes.

2.4 | Data analysis and statistics

Patients, primary diagnosis, treatment, and hospital stay were described as well as the incidence of delirium. The mean serum levels of CRP during admission in patients without delirium were compared to the last measured CRP serum level for patients with delirium before the onset of symptoms. To compare the patients with a delirium versus those without, and to search for characteristics, univariate and multivariate logistic regression analyses were performed to estimate ORs (odds ratios) and 95%CIs (confidence intervals). Two-sided testing was used, where a P-value < 0.05 was considered to be statistically significant. All potential baseline characteristics were included in univariate analysis. Predictors with a P-value of <0.15 in univariate analysis were considered in a multivariate model. Step-by-step elimination of the least significant variable with backward selection was used for developing a multivariate model including only statistical significant variables. As age is a well-known factor being associated with delirium, age was forced into the model. To estimate associations between delirium and other complications (ORs and 95%CIs) logistic regression analyses were performed. To control for confounding with other complications than delirium, this variable was included in the multivariate regression models. Statistical

analyses were performed using IBM SPSS software, version 23.0 (IBM Corporation, Armonk, NY).

3 | RESULTS

A total of 136 patients were included in the analysis. Median age of those undergoing CRS-HIPEC was 60 years (range: 18-76) and 50 (37%) patients were male (Table 1). The median BMI was 24 (range: 11.5-54.3). A majority of 104 (76.4%) patients were diagnosed with a colorectal carcinoma as primary tumor. The surgical procedure of 68 (50%) patients lasted more than 9 h. Twenty-seven (21%) patients needed 1-3 packed cells transfusions, 25 (19%) patients needed 3-6 packed cells transfusions, and 8 (6%) patients more than 6 packed cells transfusions. Complete cytoreduction was achieved in 103 (77.4%) patients

TABLE 1 Patient, tumor, and surgery characteristics (n = 136)

	All patients	Non-delirious patients	Delirious patients
Demographic characteristics			
Number (n)	136	98	38
Age (years) median (range)	60 (18-76)	58 (26-74)	63 (18-76)
Male sex % (n)	37% (50)	37.8% (37)	34.2% (13)
BMI median (range)	24 (11.5-54.3)	24.2 (11.5-40.0)	24 (14.4-54.3)
ASA score median (range)	2 (0-3)	2 (0-3)	2 (0-3)
Age adjusted Charlson comorbidity (1) % (n)	7.4% (10)	5.1% (5)	13.2% (5)
Hypertension % (n)	21.3% (29)	15.3% (15)	36.8% (14)
Diabetes mellitus II % (n)	2.2% (3)	2.0% (2)	2.6% (1)
Tumor and surgery characteristics			
Length of surgery (h) % (n)			
≤9	50% (68)	58.2% (57)	28.9% (11)
>9	50% (68)	41.8% (41)	71.1% (27)
Tumor type % (n)			
Colon/adeno/rectal carcinoma	76.5% (104)	76.5% (75)	76.3% (29)
Pseudomyxoma peritonei (disseminated peritoneal adenomucinosis)	14.7% (20)	16.3% (16)	10.5% (4)
Pseudomyxoma peritonei (peritoneal mucinous carcinomatosis)	2.9% (4)	3.1% (3)	2.6% (1)
Ovarian carcinoma	1.5% (2)	1.0% (1)	2.6% (1)
Intraperitoneal mesothelioma	3.7% (5)	3.1% (3)	5.3% (2)
Tubulo papillary mesothelioma	0.7% (1)	–	2.6% (1)
Peritoneal cancer index % (n)			
0-21	81.7% (58)	84.4% (38)	76.9% (20)
22-39	18.3% (13)	15.6 (7)	23.1% (6)
Number of packed cells transfusions % (n)			
No packed cells transfusion	54.2% (71)	58.8% (55)	43.2% (16)
1-3 packed cells transfusions	20.6% (27)	19.1% (18)	24.3% (9)
3-6 packed cells transfusions	19.1% (25)	17.0% (16)	24.3% (9)
More than 6 packed cells transfusions	6.1% (8)	5.3% (5)	9.1% (3)
Number of organs resected % (n)			
0-2	30.1% (41)	37.8% (37)	10.5% (4)
3-7	69.9% (95)	62.2% (61)	89.5% (34)
HIPEC regimen mitomycine C	94.1% (128)	93.9% (92)	94.7% (36)
Completeness of cytoreduction score			
0	77.4% (103)	77.1% (74)	78.4% (29)
1	18.0% (24)	18.8% (18)	16.2% (6)
2	2.3% (3)	2.1% (2)	2.7% (1)
3	2.3% (3)	2.1% (2)	2.7% (1)

TABLE 2 Postoperative patient characteristics (n = 136)

Admission characteristics	All patients	Non-delirious patients	Delirious patients
Number (n)	136	98	38
Length of hospital stay (days) median (range)	16 (4-53)	15 (6-53)	21 (10-49)
Mental status change % (n)	33.8% (46)	8.2% (8)	100% (38)
Delirium	28% (38)	–	100% (38)
Other	6% (8)	8.2% (8)	–
C-Reactive Protein (mg/L) median (range)	85.5 (10-341)	78 (28-289)	109 (10-341)
Highest CRP during admission (mg/L)			
<150	39.8% (53)	44.8% (43)	27% (10)
>150	50.2% (80)	55.2% (53)	73% (27)
Highest CRP first 7 days post-operative (mg/L) median (range)	155 (44-364)	151 (44-364)	165 (52-341)
Clavien Dindo complication classification			
Grade I	19.1% (26)	20.4% (20)	15.8% (6)
Grade II	29.4% (40)	23.5% (23)	44.7% (17)
Grade III	13.2% (18)	10.2%(10)	21.1% (8)
Grade IV	2.9% (4)	3.1% (3)	2.6% (1)
Grade V	1.5% (2)	1.0% (1)	2.6% (1)

and Mitomycine C was used as HIPEC regimen in 128 (94.1%) patients. Median length of hospital stay was 16 days (range: 4-53) (Table 2). All patients received an epidural catheter containing levobupivacaine and sufentanil preoperatively, for postoperative analgesia.

3.1 | The incidence of delirium

During hospitalization, 46 (34%) patients experienced mental status change, of which 38 (28%) patients were diagnosed with delirium. Other presentations, besides delirium, were mainly shortly disorganized thinking and hallucinations, with consciousness of the patient. Psychiatrists were consulted to evaluate the patients with delirium in 25 (65.8%) cases. The chart-based instrument for delirium during hospitalization identified two more patients who were suspicious for delirium. Haloperidol (an antipsychotic drug) was prescribed for 31 (88.6%) patients with delirium. Most patients developed delirium in the first 7 days after surgery (see Figure 1).

3.2 | Postoperative complications

Postoperative complications were classified for the hospitalized postoperative period and are shown in Table 2. Complications rates were higher among the group of patients with postoperative delirium (86.8%) compared to those without (58.2%). Grade II complications were most frequently seen in both groups, followed by grade I complications in patients without delirium and grade III complications in patients with delirium. Sepsis occurred in 6 (15.8%) patients

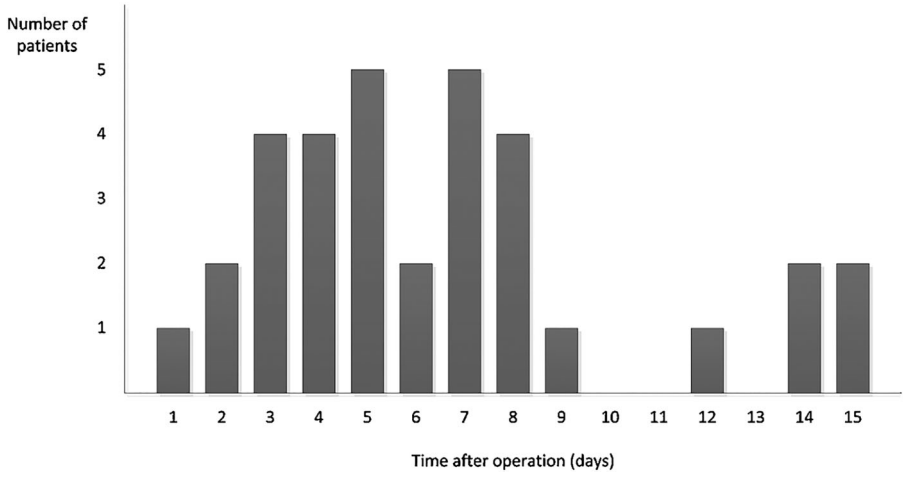

FIGURE 1 Time of postoperative delirium onset shown for the first 15 days

with delirium in contrast to 1 (1%) patient without delirium. Other reported infectious postoperative complications were line sepsis in 7 (5.1%) patients, wound infection in 5 (3.7%) patients and urinary tract infection in 10 (7.4%) patients. In the postoperative course, electrolyte derangement (hyponatremia or hypokalemia) was observed in 11 (8.1%) patients of which 1 (0.7%) patient had hyponatremia. The chance of postoperative delirium is five times greater in those patients with any other postoperative complication (OR: 4.75; 95% 1.71-13.20) and in patients with postoperative electrolyte derangements (OR: 5.31; 95% 1.46-19.35). In patients with sepsis the chance on postoperative delirium during admission is 18 times greater than in those without sepsis (OR: 18.19; 95% 2.11-156.82) (Table 3).

3.3 | C-reactive protein

Median CRP peak serum levels were 155 (44-364) mL/g during the first 7 days after surgery and 180 (25-569) mL/g during admission. All patients showed an increase in CRP serum level in the postoperative period with a median of 78 (28-289) mL/g for the patients without delirium and a median of 109 (10-341) mL/g for those diagnosed with delirium.

3.4 | Characteristics associated with delirium

Univariate logistic regression showed that the more organs were resected, the greater the chance of developing delirium after surgery (Table 4). More detailed analysis showed that the difference was significant between 0 and 2 organs resected versus 3-7 organs resected (OR: 5.16; 95% 1.69-15.70, $P = 0.004$). The length of the surgical procedure overall was longer for patients with delirium compared to the patients without delirium, where surgery lasting longer than 9 h was associated with an increased risk of developing a delirium (OR: 3.41; 95% 1.52-7.65, $P = 0.003$). Patients with delirium more often suffered from hypertension as a comorbid condition (OR: 3.23; 95% 1.37-7.62, $P = 0.007$). Serum levels of CRP, as described in methods, were higher in patients with postoperative delirium (OR: 1.01; 95% 1-1.01, $P = 0.01$). Multivariate logistic regressions showed that after adjustment for age and complications other than delirium, having three or more organs resected (OR: 3.97; 95% 1.24-12.76, $P = 0.02$) and a higher serum level of CRP (OR: 1.01; 95% 1-1.01, $P = 0.04$) were independent significant predictors for postoperative delirium (Table 5), with age included in the model (OR: 1.61; 95% 0.64-4.05, $P = 0.31$). Even after exclusion of 7 (5.1%) patients that developed sepsis in the postoperative period (to avoid confounding) from additional regression analysis, the mentioned predictors were still significant in the multivariate model; after adjustment for age and complications other than delirium, having three or more organs resected (OR: 3.38; 95 % 1.04-11.01, $P = 0.04$) and a higher serum level of CRP (OR: 1.01; 95% 1.0-1.02, $P = 0.03$), with age included in the model (OR: 1.60; 95% 0.60-4.33, $P = 0.35$).

4 | DISCUSSION

This report shows an incidence of 28% (95%CI 0.20-0.36) of postoperative delirium occurring after CRS-HIPEC. The main predictors for postoperative delirium were the number of organs resected during surgery and the serum level of CRP before the diagnosis of delirium. Age was not identified as independent predictor for postoperative delirium.

4.1 | Incidence of postoperative delirium

In other studies, the incidence of postoperative delirium varies among different surgical procedures with an incidence of 14.1% in elderly patients with colorectal cancer after surgery, 26.3% in patients after major head and neck surgery, and 50% in patients after esophagectomy.[16–18] The incidence of delirium in this study is comparable with the incidence reported for major surgery in other fields. Due to the fluctuating course and the different subtypes of delirium, the diagnosis of delirium is estimated to be missed in 75% of cases according to the literature.[9] Therefore, it is plausible to assume that in reality the incidence of delirium after surgery is higher than noted in the previous studies. In particular, the hypoactive subtype of delirium is hard to recognize by clinical staff, since the clinical features consist of fatigue and lack of activity, which can easily be mistaken for sleepiness.[10,19]

Besides delirium, other mental status changes were found in our study, but did not reach the criteria according the DSM-IV for delirium. This could indicate that CRS-HIPEC has influence on mental status and emotions, but emotional functioning was not

TABLE 3 Associations between postoperative complications and delirium ($n = 136$)

Variable	All patients	Non-delirious patients	Delirious patients	Odds ratio	95%CI	*P*
Postoperative complications (without delirium) % (*n*)	66.2% (90)	58.2% (57)	86.8% (33)	**4.75**	**1.71-13.20**	**0.003**
Electrolyte derangement	8.1% (11)	4.1% (4)	18.4% (7)	**5.31**	**1.46-19.35**	**0.01**
Sepsis	5.1% (7)	1.0% (1)	15.8% (6)	**18.19**	**2.11-156.82**	**0.008**
Line sepsis	2.2% (3)	2.0% (2)	2.6% (1)	1.30	0.11-14.74	0.83
Wound infection	3.7% (5)	3.1% (3)	5.3% (2)	1.76	0.28-10.97	0.55
Urinary tract infection	7.4% (10)	6.1% (6)	10.5% (4)	1.80	0.48-6.79	0.38

Bold values are considered significant. (*P* value < 0.05).

TABLE 4 Predictors for the occurrence of a delirium after HIPEC, univariate logistic regression

Variable	Odds ratio	95%CI	*P*
Age (years)			
≤65	1		
>65	1.90	0.86-4.21	0.11
Sex			
Female	1		
Male	1.17	0.53-2.56	0.70
BMI	1.04	0.98-1.01	0.23
ASA score			0.73
1	1		
2	1.07	0.26-4.45	0.92
3	0.70	0.11-4.54	0.71
Age adjusted Charlson comorbidity	2.82	0.77-10.36	0.12
Hypertension			
No	**1**		
Yes	**3.23**	**1.37-7.62**	**0.007**
Diabetes mellitus II			
No	1		
Yes	1.30	0.11-14.74	0.83
Length of surgery (h)			
≤9	**1**		
>9	**3.41**	**1.52-7.65**	**0.003**
Peritoneal cancer index			
≤21	1		
>22	1.63	0.48-5.50	0.43
Number of packed cells transfusions			0.28
No packed cells transfusion	1		
1-3 packed cells transfusions	1.72	0.65-4.56	0.28
3-6 packed cells transfusions	1.96	0.80-4.84	0.14
Number of organs resected			
≤2	**1**		
>3	**5.16**	**1.69-15.70**	**0.004**
Complete cytoreduction			
Yes	1		
No	0.93	0.37-2.32	0.87
C-reactive protein (mg/L)	**1.01**	**1-1.01**	**0.01**

Bold values are considered significant. (*P* value < 0.05).

investigated in this study. A study which reported the recovery process of patients who underwent CRS-HIPEC, described that 49 of 76 (64%) patients suffered from anxiety, worry, feeling down or abandoned, and had hallucinations during the first 3 postoperative weeks.[7]

4.2 | The inflammatory response

Surgical trauma is an initiator of an inflammatory response.[11] The data accumulated in the course of this study show an enormous rise of postoperative serum levels of CRP. This reflects the strong inflammatory response that occurs after the CRS-HIPEC procedure, as stated in earlier research.[20] The possibility of a link between CRP levels and delirium has been described, but published data are contradictory.[21–26] In our study, the extensive rise of CRP after CRS-HIPEC, indicating systemic inflammation, was seen and serum level of CRP was found as in independent predictor for delirium.[27]

Earlier research showed that a prolonged length of surgery was associated with a higher risk for postoperative delirium.[28–31] Our study showed similar results, in the group of patients with postoperative delirium, the length of surgery was longer than in the group of patients who did not experience postoperative delirium. This may be related to increased doses of anesthetic medicine and greater volumes of blood transfusion, with increased chance of hypo perfusion and systemic inflammatory response.[30] A relation between the increased systemic inflammatory response and prolonged length of surgery is important in sight of a possible association between the inflammatory response and postoperative delirium as earlier described. The increased length of surgery may predispose patients to delirium because of increased cytokines release.[31,32]

An association between intraoperative blood loss and subsequent packed cells transfusions and the occurrence of delirium after surgery has been described in a few studies.[32,33] Packed cells transfusion is described as a strong predictor for early postoperative delirium. Intraoperative transfusions of larger volumes of blood have repeatedly been linked to postoperative delirium.[34] Although other studies have shown that patients who developed delirium had greater intraoperative blood loss and received more postoperative transfusions, this association was not found in our study.[35] It has been described that packed cells transfusion triggers an inflammatory response which has been shown to directly increase plasma concentrations of inflammatory mediators.[36] In our study, a difference in inflammatory response for CRP between the patients with delirium and without delirium was found.[34]

Taken together, the findings in our study underscore the hypothesis of neuroinflammation as mechanism underlying the pathophysiology of delirium. Surgery initiates a systemic inflammatory response that can disrupt the function of multiple organs, including the brain.[37] The exaggerated neuro-inflammatory response may damage neurons, resulting in postoperative cognitive deterioration, like delirium.

4.3 | Postoperative complications and delirium

The length of hospital stay of patients with postoperative delirium was longer than the length of hospital stay of patients who did not experience delirium. Prolonged hospital stay after postoperative

TABLE 5 Predictors for the occurrence of a delirium after HIPEC, multivariate logistic regression

	All patients (*n* = 136)			Sepsis excluded (*n* = 129)		
Variable	**Odds ratio**	**95%CI**	***P***	**Odds ratio**	**95%CI**	***P***
Age (years)						
≤65	1			1		
>65	1.61	0.64-4.05	0.31	1.60	0.60-4.33	0.35
Number of organs resected						
≤2	**1**			**1**		
>3	**3.97**	**1.24-12.76**	**0.02**	**3.38**	**1.04-11.01**	**0.04**
C-reactive protein (mg/L)	**1.01**	**1-1.01**	**0.04**	**1.01**	**1.0-1.02**	**0.03**
Complications without delirium						
No	**1**			1		
Yes	**3.82**	**1.19-12.30**	**0.03**	3.22	0.99-10.51	0.05

Bold values are considered significant. (*P* value < 0.05).

delirium is frequently seen in other studies and is associated with an increase in postoperative complications.[17,38,39] CRS-HIPEC comes with a high incidence of postoperative complications, also observed in our study.[2] Delirium and complications can co-exist, but the relation of delirium and other postoperative complications has not been well-examined. In the current study, the incidence rate of severe complications in patients with delirium was higher than in patients without delirium.

4.4 | Age and comorbidities

Age was not an independent predictor for postoperative delirium, in contrast to the literature were age >70 years is described as a risk factor.[40] In our study, few patients were aged 70 years or over, which might be an explanation for not reaching significance in multivariate analysis. As has been shown in other studies, in this study patients with delirium more often suffered from hypertension than the patients who did not develop a delirium.[33,41] Hypertension possibly is a sign of increased vascular risk and may be indicative of vascular brain damage, making patients more vulnerable to conditions such as delirium.[39,42] A similar effect of diabetes mellitus was not seen in the current study, probably due to the low incidence in the population.

4.5 | Critical evaluation of the study

Although the present study provided novel information about postoperative delirium following CRS-HIPEC, there were a number of study limitations. First, an obvious limitation is the use of the chart-based method to identify patients with diagnosed and undiagnosed delirium, which mainly searches for hyperactive delirium.[14] It might be possible that the hypoactive delirium was missed which may imply a higher incidence of delirium in reality, than found in our study. However, the chart-based method was used in addition to clinical diagnosis by a psychiatrist or specialist in elderly medicine. Second, for this study, we used a retrospective chart review, which is limited by the quality of the documentation in the charts. Third, more accurate data on opioid and/or narcotic use in the postoperative period than epidural use, were not available in this study. In a more ideal setting, a prospective analysis would overcome this weaknesses, and reliable data about the subtypes of delirium can be reported.

4.6 | Unanswered questions and future research

Neuroinflammation is among the most popular hypothesized mechanism underlying the pathophysiology of delirium. Pro-inflammatory markers are associated with the development of delirium in relative healthy elderly.[43] However, the production of CRP, which is elevated in inflammation and infection, is under control of other cytokines. It may be that the levels of more specific cytokines are more closely related with the process of systemic inflammation, than CRP is. These cytokines could be more interesting for further research.[32] Concerning the relation between postoperative complications and delirium, cause and effect remain unclear. Whether a postoperative delirium increases the risk for other postoperative complications or whether a postoperative delirium is a symptom of other complications which can occur after surgery, remains to be clarified and further research is needed.

5 | CONCLUSIONS

In conclusion, this retrospective analysis shows an incidence of 28% of postoperative delirium, occurring after CRS-HIPEC. Surgery extensiveness and serum level of CRP were independent predictors for delirium postoperatively, when correcting for age and complications other than delirium. An extensive inflammatory response occurs after CRS-HIPEC, represented by elevated serum CRP levels. The process of systemic inflammation and the relation with levels of cytokines and delirium requires further research.

CONFLICTS OF INTEREST

The authors report no proprietary or commercial interest in any concept discussed in this article.

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